PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Mental health in the second year of the COVID-19 pandemic: Protocol for a nationally representative multilevel survey in Serbia
AUTHORS	Marić, Nadja P.; Lazarević, Ljiljana B.; Mihić, Ljiljana; Pejovic Milovancevic, M; Terzić, Zorica; Tošković, Oliver; Todorović, Jovana; Vuković, Olivera; Knezevic, Goran

VERSION 1 – REVIEW

REVIEWER	Calvano, Claudio Free University of Berlin
REVIEW RETURNED	16-Jul-2021

GENERAL COMMENTS	Thank you for the opportunity to review the study protocol entitled "Protocol of the national representative survey of mental health in the second year after the COVID-19 outbreak: Multilevel analysis of individual and societal factors". The protocol is well-written, background and methods are sufficiently described. In encourage the authors to add a discussion or conclusion section to the abstract, as in its current form, it a bit unbalanced. The method section need a reference on the time frame of data collection. Further, woh is conduction the random sampling?

REVIEWER	Fiorillo, Andrea University of Campania Luigi Vanvitelli
REVIEW RETURNED	17-Jul-2021

GENERAL COMMENTS	This is an interesting reserach protocol which is going to be carried out in Serbia with an innovative design, although the topic of the effects of COVID-19 on mental health has been widely explored. It is not clear how the sample size was calculated. Other studies carried out in China and in Europe should be confronted. Among mediating factors, other authors have found the role of loneliness, resilience, use of Internet, employment and female gender. Moreover, the presence of mental health problems prior to the pandemic is consistently reported as one of the most important predictive factors. These should be either added to the analyses or discussed or acknowledged among the study limitations. How the authors will deal with drop outs? Would it be possible to carry on a longitudinal assessment, with two or three evaluations, in order to detect possible changes? In the aftermath of the COVID-19, the long-COVID syndrome is emerging as affecting the mental health status of affected people. I

	would suggest the authors to include an evaluation of cognitive deficits and, possibly, fRMI in a subsample in order to verify the presence of cognitive deficits.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Claudio Calvano, Free University of Berlin

Comments to the Author:

Thank you for the opportunity to review the study protocol entitled "Protocol of the national representative survey of mental health in the second year after the COVID-19 outbreak: Multilevel analysis of individual and societal factors". The protocol is well-written, background and methods are sufficiently described.

Thank you very much for positive feedback. We would also like to thank you for your time and effort aimed to improve our protocol paper. We carefully addressed all issues raised and revised the manuscript accordingly.

*I encourage the authors to add a discussion or conclusion section to the abstract, as in its current form, it is a bit unbalanced. [NOTE FROM THE EDITORS: PLEASE REBUT THIS REQUEST - WE DO NOT INCLUDE DISCUSSION OR CONCLUSION SECTIONS IN THE ABSTRACTS OF PROTOCOL PAPERS]

*The method section need a reference on the time frame of data collection. Further, who is conduction the random sampling?

We added the time frame of data collection in both Abstract and in the Method section. Random sampling was done by two statisticians, both members of the authors' team (this information is available in the Authors contribution statement). The selection of the settlements and municipalities from which respondents will be recruited was based on the random selection from the database created by the Statistical Office of the Republic of Serbia (database includes information on the name of the settlement, municipality, region, and the number of inhabitants).

Reviewer: 2

Dr. Andrea Fiorillo, University of Campania Luigi Vanvitelli

Comments to the Author:

This is an interesting research protocol which is going to be carried out in Serbia with an innovative design, although the topic of the effects of COVID-19 on mental health has been widely explored.

Thank you for positive evaluation of our manuscript and for taking time to review it. We revised the manuscript in line with all your comments and suggestions.

*It is not clear how the sample size was calculated.

*The sample size was calculated based on the power analysis. One of the main strategies of data analysis would be to correlate assessment of virus exposure to various indices of mental health status. The sample size of 1200 participants enables detecting the correlation of .08 with power of 0.80 (and with alpha level set at 0.05). It means that if 1% of the variance is shared between mental health indices and Covid19 exposure, the design of our study enables detecting it. The sample size of our study enables detecting the difference in the overall prevalence of mental health diagnoses - between those with history of CoV2-infection (or showing COVID-19 distress) - of the size that was reported by the recent Czech study (Winkler et al., 2020) with the power of .80 (at the .05 alpha level). For example, the odds ratio of 2.13 to be diagnosed with any mental disorder among those tested for the virus, compared to those not tested, has been reported in the Czech study. Assuming that 10% of the population underwent the test (incidence of Covid-19 in Serbia) and that 20% of those not tested are diagnosed with any mental disorder, the required total sample size to detect the effect of the size reported in Czech study is 751 (at 0.5 alpha level). It means that our sample size has power of .94 to detect it (G*power), or that a smaller odds ratio of 1.85 would be still possible to detect with our sample size, with power of .80, and 0.05 alpha level (of notice, with the rise of the number of individuals tested, the power also rises). In our study, we have so called COVID-19 exposure variables elaborated in more details (Cov-2 related situational risks, 9 item questionnaire) capturing potentially more stressful Cov-2 related experiences (such as hospital treatment of a participant or her/his close others). Apart from this, the justification for this sample size from the point of view of multilevel modeling is also presented on p. 4.*

*Other studies carried out in China and in Europe should be confronted.

To the best of our knowledge, only one study recruited a nationally representative sample to use an established psycho-diagnostic instrument - structured interview - to detect MH disorders prevalence in relation to the COVID-19 pandemic and this study (Czech republic) was mentioned. However, when we noticed that the majority of the published studies have been conducted online within the first months of the pandemic, and have mostly relied on diagnostic screening tools or diagnostic questionnaires with a short reference period., we missed to add citations. Thus, we will use this opportunity to add two European studies (included, p. 3):

McCracken, L., Badinlou, F., Buhrman, M., & Brocki, K. (2020). Psychological impact of COVID-19 in the Swedish population: Depression, anxiety, and insomnia and their associations to risk and vulnerability factors. European Psychiatry, 63(1), E81. doi:10.1192/j.eurpsy.2020.81

Fiorillo, A., Sampogna, G., Giallonardo, V., Del Vecchio, V., Luciano, M., Albert, U., . . . Volpe, U. (2020). Effects of the lockdown on the mental health of the general population during the COVID-19 pandemic in Italy: Results from the COMET collaborative network. European Psychiatry, 63(1), E87. doi:10.1192/j.eurpsy.2020.89

*Among mediating factors, other authors have found the role of loneliness, resilience, use of Internet, employment and female gender. Moreover, the presence of mental health problems prior to the

pandemic is consistently reported as one of the most important predictive factors. These should be either added to the analyses or discussed or acknowledged among the study limitations.

Thank you for this comment which emphasises the importance of different mediating factors. We completely agree that this list of mediators should be addressed, therefore we have already included all of them (p. 6).

To explore loneliness, we included the scale provided by Hughes ME, et al, 2004 Nov;26(6):655-72.

To explore strength and capacity for resumption of normal functioning during and after COVID related stresses, we included questions how the COVID-19 pandemic influenced different areas of lives at the time of the assessment, providing participants to answer if family relations, friendships, work/studies, physical activity, financial situation and ***internet use*** *were affected in positive, neutral or negative direction (scale 1-5) - instrument* ***Perception of COVID-19 pandemic consequences*** *on various aspects of life, which has been mentioned shortly, but we will now add more detailed information.*

Information about the employment status and sex will be provided trought the ***Socio-demografic questionairre.***

For presence of MH problems prior to the pandemic, we will check for pre-existing psychiatric conditions (health status variables). In addition, we will explore the use of anxiolytics and hypnotics focusing on the period before and during the pandemic, and 7 days preceding the assessment.

*How the authors will deal with drop outs?

There will be no available information about the non-responders, and we will not be able to conclude about this group of people, which could influence our results. This is now added to the limitation section (p.8).

*Would it be possible to carry on a longitudinal assessment, with two or three evaluations, in order to detect possible changes?

This is a very useful comment and we fully agree with you that running a longitudinal study is the state-of-the art design. At the moment, we have not submitted any protocol for the follow up (the present protocol was approved only for the cross sectional study). Nevertheless, we would be very interested to continue working on this topic and run repeated assessments if there is an opportunity to get sufficient support.

*In the aftermath of the COVID-19, the long-COVID syndrome is emerging as affecting the mental health status of affected people. I would suggest the authors include an evaluation of cognitive deficits and, possibly, fRMI in a subsample in order to verify the presence of cognitive deficits.

Again, we fully agree with you that exploration of neurobiological underpinnings of MH status would be great. Unfortunately, we don't have resources to do it, and our funding body is sponsoring only data collection described in the manuscript. However, we are very willing and interested to include those measurements in our future studies and collaborations.

VERSION 2 – REVIEW

REVIEWER	Fiorillo, Andrea University of Campania Luigi Vanvitelli
REVIEW RETURNED	02-Sep-2021

GENERAL COMMENTS	Thank you for this revised version of the paper. I would suggest some minor changes in order to further improve the quality of the paper: 1. in the introduction, authors should consider to clarify the impact and the relevance of the pandemic on mental health and on mental health professionals responsibilities (some relevant papers have been recently published and should be quoted such as Stewart DE, Appelbaum PS. COVID-19 and psychiatrists' responsibilities: a WPA position paper. World Psychiatry. 2020;19(3):406-407; Fiorillo A, Gorwood P. The consequences of the COVID-19 pandemic on mental health and implications for clinical practice. European Psychiatry; 2020;63(1):e32; Adhanom Ghebreyesus T. Addressing mental health needs: an integral part of COVID-19 response. World Psychiatry. 2020;19(2):129-130). 2. a specific comment should be added on the phenomenon of the "COVID-19 health anxiety", since this should represent a very relevant issue in the long-term of the pandemic (please see Tyrer P. COVID-19 health anxiety. World Psychiatry. 2020;19(3):307-308). 3. among contextual and socio-demographic factors , authors did not include any information related to the cognitive impairment/dysfunction which should be present in people infected with COVID. These cognitive aspects (the so-called "neuro-COVID") are very relevant also for mental health and well being. Authors should discuss on this issue. 3. In the final part of the discussion, clinical implications should be discussed in more details, even considering some quotations such as Kuzman MR, Curkovic M, Wasserman D. Principles of mental health care during the COVID-19 pandemic. European Psychiatry; 2020;63(1):e45; Gorwood P, Fiorillo A. One year after the COVID-19: What have we learnt, what shall we do next? Eur Psychiatry. 202115;64(1):e15.; Thome J, Coogan AN, Simon F, Fischer M, Tucha O, Faltraco F, et al. The impact of the COVID-19 outbreak on the medico-legal and human rights of psychiatric patients. European Psychiatry; 2020;63(1):e50; Marazziti D, Stahl SM. The relevance of COVID-19 pandemic to psychiatry. World Psychiatry. 2020;19(2):261.)

VERSION 2 – AUTHOR RESPONSE

#Reviewer

1. in the introduction, authors should consider to clarify the impact and the relevance of the pandemic on mental health and on mental health professionals responsibilities (some relevant papers have been recently published and should be quoted such as Stewart DE, Appelbaum PS. COVID-19 and psychiatrists' responsibilities: a WPA position paper. World Psychiatry. 2020;19(3):406-407; Fiorillo A, Gorwood P. The consequences of the COVID-19 pandemic on mental health and implications for clinical practice. European Psychiatry; 2020;63(1):e32; Adhanom Ghebreyesus T. Addressing mental health needs: an integral part of COVID-19 response. World Psychiatry. 2020;19(2):129-130).

Thank you, we added the sentences according to the suggestion, fourth paragraph, p. 3.

2. a specific comment should be added on the phenomenon of the "COVID-19 health anxiety", since this should represent a very relevant issue in the long-term of the pandemic (please see Tyrer P. COVID-19 health anxiety. World Psychiatry. 2020;19(3):307-308).

Thank you for this comment. Upon your suggestion, we now explicitly mentioned COVID-19 health anxiety in the discussion (p.7). Namely, one of the instruments used in our study (Covid Stress Scale - CSS) is measuring subdomains:

- *fear of contamination by COVID-19,*
- *traumatic stress symptoms associated with direct or indirect exposure to the virus and COVID-19,*
- *related compulsive checking and reassurance seeking,*

which correspond to the COVID-19 health anxiety described by Tyrer (2020) ("those with severe health anxiety are likely to become abnormally avoidant, , who continuing to isolate and practise repeated hand washing, checking their body temperatures, respiratory function, and even testing their ability to smell (as this is a recognized symptom of the infection) over and over again. There is considerable overlap between obsessional symptomatology and health anxiety, and a relentless concern with safety seeking behaviours may come to dominate some people's lives").

From the title of the CSS it is not obvious that this instrument measures the health-anxiety concerns. Now, we stated this in the discussion more clearly. An advantage of using the CSS is that it assesses COVID-19 related distress not as a specific phobia or narrow anxiety-related issue but as a multifaceted phenomenon (Asmundson & Taylor, 2020).

3. among contextual and socio-demographic factors , authors did not include any information related to the cognitive impairment/dysfunction which should be present in people infected with COVID. These cognitive aspects (the so-called "neuro-COVID") are very relevant also for mental health and well being. Authors should discuss on this issue.

We agree that the assessment of cognition is relevant, however this is beyond the scope of the present study and exceeds our approved funding. However, we acknowledged this in the Discussion section, first paragraph, p. 8.

4. In the final part of the discussion, clinical implications should be discussed in more details, even considering some quotations such as Kuzman MR, Curkovic M, Wasserman D. Principles of mental health care during the COVID-19 pandemic. European Psychiatry; 2020;63(1):e45; Gorwood P, Fiorillo A. One year after the COVID-19: What have we learnt, what shall we do next? Eur Psychiatry. 202115;64(1):e15.; Thome J, Coogan AN, Simon F, Fischer M, Tucha O, Faltraco F, et al. The impact of the COVID-19 outbreak on the medico-legal and human rights of psychiatric patients. European Psychiatry; 2020;63(1):e50; Marazziti D, Stahl SM. The relevance of COVID-19 pandemic to psychiatry. World Psychiatry. 2020;19(2):261.)

Thank you very much for highlighting this important aspect of medical care. We added the following text to the Discussion section, last paragraph, p. 8.

"In particular, limited access to MH care due to unavailability of MH services could negatively impact adequate diagnostic and therapy (Holmes et al, 2020). Present study will be able to provide clinically relevant information about the unmet needs of the population."